RISK FACTORS FOR FIRST STROKE IN WOMEN LESS THAN 50

Aamir Shahzad, Shahid Abbasi, Amjad Nasim, Sumera Gul

Department of Medicine,
Foundation University Medical College Rawalpindi - Pakistan

ABSTRACT

Objectives: *To determine the risk factors of first stroke in young women.*

Material and Methods: *Thirty seven young female patients admitted in medical ward were included. Clinical assessment and relevant investigations were carried out to identify the frequency of various risk factors.*

Results: *Out of these 37 patients, 8 (21%) had hemorrhagic stroke and 29 (79%) had ischemic stroke. Valvular heart disease was the most important risk factor for stoke and seen in 15 (51.7%) of ischemic stroke followed by hypertension and diabetes mellitus in 6 patients each (20.6% each) Mitral stenosis was the most common cardiac lesion. In hemorrhagic stroke, 5 (62.5%) had valvular heart disease and the presented with intracranial bleeding due to warfarin toxicity. One patient (12.5%) had hypertension and one (12.5%) vascular malformation.*

Conclusion: *Valvular heart disease is the most common risk factor observed for first stroke in young females, (51.7%) followed by hypertension (20.6%) and diabetes mellitus (20.6%) each.*

Key words: *Stroke, Young females, Risk factors*

INTRODUCTION

Stroke is the leading cause of adult disability and is the third commonest cause of death worldwide[1]. More than two-thirds of the global burden of stroke is borne by developing countries, where the average age of patients with stroke is 15 years younger than in developed countries[2]. The available limited data indicates that stroke occurring in young people in developing countries is more often atherothrombotic in origin[3]. In contrast in developed countries arterial dissection and cardioembolic aetiologies predominate[4, 5].

In Pakistan various studies have been performed to analyze the risk factors in young patients. A major study from Karachi reported Hypertension, smoking, hyperlipidemia and a family history of stroke as the major risk factors[6].

However all these studies were conducted in both male and female patients. To the best of our knowledge no study was performed on female patients only. We planned this study mainly to analyze this group of patients and to compare these results with national and international studies.

MATERIAL AND METHODS

This study was conducted at Fauji Foundation Hospital Rawalpindi. It is a descriptive study completed in almost three years (Jan 2006-Oct 2008). Informed consent was taken either from patients or the next of kin. A total of 37 young women between 12 to 45 years of age were included, all patients admitted in medical ward with acute neurological deficit with a clinical diagnosis of stroke. Only those patients were included who reported first such attack of their life.

A detailed clinical assessment was done at the time of admission. All the patients were investigated by blood complete examination, urine examination. Biochemical profile included renal function tests, blood sugar, lipid profile, PT, aPTT, and liver functions tests. CT scan brain was done in every patient. Echocardiogram was done in

TYPES OF STROKE

Type of Stroke	No Patients n= 37
Intracranial bleeding	7 (18.9%)
Subarachnoid hemorrhage	1 (2.7%)
Ischemic stroke	29 (79%)

Table 1

selected patients who had some cardiac problem on examination. In one patient, who had a carotid bruit, Doppler ultra sound for carotid arteries was also requested. Homocystin levels were not done in any patient as we planned to check it only in those patients where no obvious risk factor would be found.

RESULTS

A total of thirty seven female patients were included in study with an age range of 17-44 years with a mean of 31.5 years. Out of these 37 patients, 8 (21%) had hemorrhagic stroke and 29 (79%) had ischemic stroke. (Table I)

Among those with hemorrhagic stroke, 7(87.5%) had intracerebral and 1(12.5%) had subarachnoid hemorrhage. Among patient with hemorrhagic stroke five (62.5%) had valvular heart disease. They were on anticoagulants and lack of control resulted in uncontrolled bleeding. INR was reported as 'failed to clot' in 3, in other two it was more than 4. Two had hypertension and they presented with hypertensive crisis resulting in intracranial bleeding. In one patient who presented with subarachnoid hemorrhage; no cause was apparent. A vascular malformation was suspected but she died before it could be confirmed.

Out of 29 patients who presented with ischemic stroke, 15 (51%) had valvular heart disease. Uncontrolled hypertension was found in 6

TYPES OF CARDIAC LESION WITH STROKE

Type of cardiac lesion	No of Patients
Mitral stenosis	9
Mitral regurgitation	3
Mitral stenosis plus Mitral regurgitation	4
Aortic regurgitation	1
Aortic stenosis	1
VSD	2

* the list includes 15 patients with ischemic stroke and 5 patients who had hemorrhagic stroke due to warfarin toxicity

Table 3

FREQUENCY OF VARIOUS RISK FACTORS IN ISCHEMIC STROKE

Risk Factors	No of Patients n= 29
Valvular heart disease	15 (51.7%)
Hypertension	6 (20.6%)
Peripartum state	1 (3.4%)
Diabetes mellitus	6 (20.6%)
carotid bruit	1 (3.4%)
family history	1 (3.4%)
vascular (meningitis)	1 (3.4%)

Table 2

patients (20.6%). Uncontrolled diabetes was present in 6 (20.6%). In one patient ((3.4%) stroke developed within a week of childbirth. In the absence of any other risk factor, she was diagnosed as a case of peripartum stroke. One patient developed stroke as a complication of pyogenic meningitis, probably a vascular involvement of meningitis. Carotid artery bruit was detected in only one patient who had diabetes and hypertension. Subsequent Doppler showed less than 50% luminal narrowing. Only one patient admitted a positive family history of cardiovascular events (in males <45 years and in females <55 years).

None of our patients had hyperlipidemia, thrombophilia(no previous personal and family history of arterial/ venous thrombosis or abortions), ischemic heart disease, SLE or antiphospholipid antibody syndrome. No patient admitted a history of smoking. (Table II). A graphic presentation of frequencies of various risk factors is shown in Graph I.

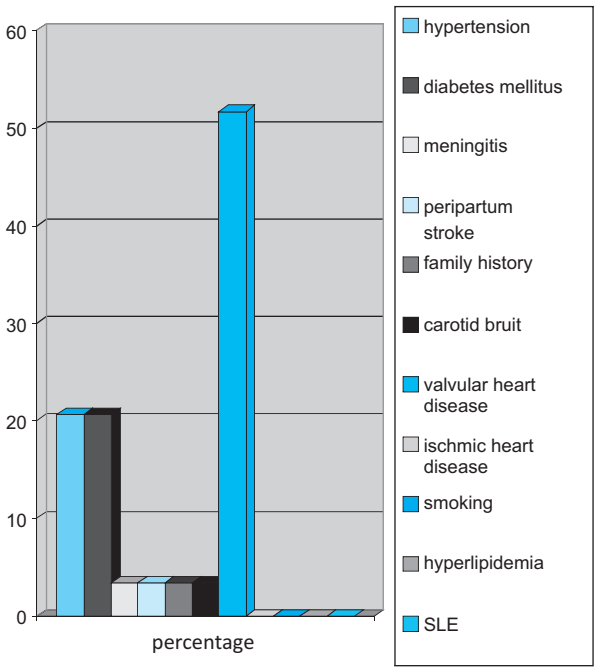
Table III shows the frequency of underlying cardiac lesions which shows Mitral stenosis as the most common lesion (24.3%).

DISCUSSION

Stroke is the third most common cause of death and the first leading cause of disability in developed and developing countries[7]. According to World Health Organization estimates, 5.5 million people died of stroke in 2002, and roughly 20% of these deaths occurred in South Asia[8]. Moreover contrary to decline in the incidence of the disease in the Western population, the burden of the disease in South Asian countries (India, Pakistan, Bangladesh, and Sri Lanka) has increased and is expected to rise further[9].

No large scale epidemiological studies are available to determine the true incidence of stroke in Pakistan. Estimated annual incidence is

FREQUENCIES OF VARIOUS RISK FACTORS IN ISCHEMIC STROKE



Graph I

250/100,000, translating to 350,000 new cases every year[10]. There is only one published stroke prevalence study from Pakistan, conducted on adult Pushtoon community residing in Karachi. This study reports a prevalence of 4.8% which was alike in men and women[11]. This is highest ever reported prevalence of stroke in the world. However, the results of this study should be interpreted with caution as a non validated questionnaire was used.

Demographics of stroke in community are lacking but hospital based studies have revealed relatively high proportion of young stroke. Khan JA et al reported that 68/260 (26%) of their patients were of 15-45 years of age[12]. Vohra et al reported that 34% of patients in their series were under age of 50 years[13]. Syed et al reported a frequency of 28% of young stroke under age of 55 years[14]. This trend is reported to be due to the fact that in developing countries ischemic heart disease present at an earlier age. An Indian study suggested that CHD manifests almost 10 year earlier on average in this region compared with the rest of the world[15].

For a disease like stroke which carries a high degree of mortality/morbidity, affliction at a young productive age is a tragedy for the person as well as the family. Efforts are required to identify the underlying risk factors with a view to plan strategy of prevention.

The profile of major modifiable risk factors is essentially similar to the one seen in stroke patients elsewhere in the world. Most common risk factors for ischemic stroke were diabetes mellitus and hypertension. Syed et al reported that approximately 77% of their cohort had diabetes mellitus, hypertension or both[14]. Various hospital - based and epidemiological studies are required to study our young population and compare the results from other international studies.

Many studies have tried to address the stroke in young Asian population. .A number of factors has been postulated to account for this high prevalence in Asia: (i) cardioembolic stroke[16] due to cardiac diseases such as rheumatic heart disease; (ii) accelerated intracranial atherosclerosis[16] (iii) arteriovenous malformations[17].

A study from India revealed that stroke in young patients accounted for 13.5%[16.] Within this group, 85.8% had ischemic stroke, while 14.2% had spontaneous intracerebral hemorrhage. Major risk factors for stroke in these patients were hypertension, hypercholesterolemia and hypertriglyceridemia. Oral contraceptives, alcohol, and illicit drug use were infrequent risk factors, in contrast to Western studies; Cardioembolic stroke (29.4%) and atherosclerotic occlusive disease (22%) were the most common causes.

A major hospital based study was reported from Karachi. They reported hypertension and ischemia as the major risk factors[18].Thirty-nine (57.35%) patients suffered ischemic stroke while 29 (42.65%) patients suffered haemorrhagic stroke. The frequency of hypertensive intracerebral haemorrhage was 32.35%, cardioembolism 20.58%, infection 11.76%, stroke related to pregnancy 19.29%, vasculitis 5.88%, atherothrombotic 4.41%, anomalous basilar artery 1.47% and secondary thrombocytosis 1.47%. Subarachnoid haemorrhage occurred in three (4.41%) of our patients. Hypertension was the most common risk factor (44.11%).

Another latest study from Karachi has also reported hypertension as the most common risk factor: The other risk factors were smoking, hyperlipidemia and family history of stroke. Cerebral infarction was diagnosed in 78(68.4%) patients and intracerebral hemorrhage/subarachnoid hemorrhage was seen in 36 (31.6%). Small vessel occlusion was common than large artery atherosclerosis. Hypertensive intracerebral hemorrhage was the most common sub-type of intra cerebral hemorrhage[19].

This study is different as we have tried to assess the risk factors in young female patients

only. To the best of our knowledge this is the first such attempt in Pakistan. Many interesting observations were noted. Like other studies reported from India[16] and Pakistan[18,19] oral contraceptives, illicit drug use and alcoholism were not significant reflecting the cultural and social trends in our population. Moreover the most significant factor observed on our study was high frequency of valvular heart disease as a source of embolic stroke. This was not reported in any other study. Out of 37 patients, 20 (54%) had underlying cardiac causes. Fifteen presented with ischemic and 5 present with intracerebral hemorrhage due to warfarin toxicity. This underscores the importance of prevention of rheumatic carditis in young population.

Hypertension was the next most important factor observed in our study. A total of 8(21.6%) patients had hypertension; 6 with ischemic and 2 with hemorrhagic stroke. This is much less than that reported from other local studies. Diabetes mellitus was observed in 20% (6). Family history, vasculitis and carotid bruit were insignificant. Obesity and metabolic syndrome were not observed in our patients.

This study, though corroborating the earlier impression that cardioembolic stroke as an important pathological basis for young stroke, differs markedly in some aspect. Hypertension was not the most important factor. Smoking, obesity and family history reported as the most important factors as by other local studies were not seen. This is probably because of two reasons. Our patients were females (lack of smoking) and our population was from poor barren areas where lack of awareness and access to medical care resulted in rheumatic carditis and warfarin over dose. Out of 15 patients with valvular heart disease who presented with ischemic stroke, 6 (6/15- 40%) were diagnosed of cardiac problem only after stroke.

Another important difference was the lack of ischemic heart disease in our patients. Earlier studies reported that the ischemic heart disease occurs at an earlier age in developing countries and this is one of the possible reasons for high percentage of young stroke[2,15]. Lack of this factor in our study is probably because our patients were only females who are relatively protected from ischemic heart disease in young age

This study has certain limitations. Being a hospital based observational study it can't replace the need for population based analysis; which is required to understand the realistic trends in our female patients. More over the number of patients was small and results can't be generalized. However it was a pilot study. The data collection is still continuing and we plan to report again with a much larger group. The idea of reporting at this stage was to draw the attention of other centers as we feel; like IHD, separate studies need to be planned in female patients for comparisons with male patients in terms of risk factors, clinical presentations and ultimate outcome.

CONCLUSION

Valvular heart disease is the most common risk factor observed for first stroke in young females, (51.7%) followed by hypertension (20.6%) and diabetes mellitus (20.6%) each.

REFERENCES

1. Bonita R, Mendis S, Truelsen T, et al. The global stroke initiative. Lancet Neurol 2004;3:391–3.
2 Truelsen T, Bonita R, Jamrozik K. Surveillance of stroke: a global perspective. Int J Epidemiol 2001;30:S11–16.
3 Garbusinski JM, van der Sande MAB, Bartholome EJ, et al. Stroke presentation and outcome in developing countries. A prospective study in the Gambia. Stroke 2005;36:1388–93.
4. Leys D, Bandu L, Henon H, et al. Clinical outcome in 287 consecutive young adults (15 to 45 years) with ischemic stroke. Neurology 2002;59:26–33.
5. Nedeltchev K, der Maur TA, Georgiadis D, et al. Ischemic stroke in young adults: predictors of outcome and recurrence. J Neurol Neurosurg Psychiatry 2005;76:191–5.
6. Makki K U, Pyar Ali Fazel, Hussain Haroon, Illahi Bakhsh Soomro. Risk factors and outcome in 114 young stroke patients. Med Channel Oct - Dec 2006;12(4):52-5.
7. Feigin VL. Stroke epidemiology in the developing world. Lancet 2005; 365: 2160-61.
8. World Health Organization (WHO). The Atlas of Heart Disease and Stroke. http://www.who.int/cardiovascular_diseases/resources/atlas/en/
9. Bulatao RA, Stephens PW. Global estimates and projections of mortality by cause. Washington, DC: Population, Health and Nutrition Department; World Bank, preworking paper 1992;1007.
10. www.pakstroke.com. An official website of Pakistan stroke society. Last accessed on April 5, 2008.
11. Jafar TH. Blood pressure, diabetes and

increased dietary salt associated with stroke-results from a community-based study in Pakistan. J Hum Hypertens 2006;20:83-85

12. Khan JA, Shah MA. Young stroke : Clinical aspects. J Coll Physicians Surg Pak 2000;10:461-66.
13. Vohra EA, Ahmed WU, Ali M. Aetiology and prognostic factors of patients admitted for stroke. J Pak Med Assoc. 2000; 50: 234-36.
14. Syed NA, Khealani BA, Ali S, Hasan A, Akhtar N, Brohi H et al. Ischemic stroke subtypes in Pakistan: the Aga Khan University Stroke Data Bank. J Pak Med Assoc. 2003; 53: 584-88.
15. Yusuf S, Hawken S, Ounpuu S, Dans T, Avesum A, Lanas F. Effect of potentially modifiable risk factors associated with myocardial infarction in 52 countries (the INTERHEART study): case-control study. Lancet 2004; 364 : 937-52
16. Mehndiratta MM, Agarwal P, Sen K, Sharma B. Stroke in young adults: a study from a university hospital in North India. Med Sci Monit 2004; 10(9):535-41.
17. Yasaka M, Minematsu K. [Stroke in young adults in Japan]. Rinsho Shinkeigaku 2005; 45(11):842-5.
18. Javaid Arif Khan, Mashoor Alam Shah. Young Stroke - Clinical Aspects J Coll Physicians Surg Pak Dec 2000;10(12):461-6.
19. Makki K U, Pyar Ali Fazel, Hussain Haroon, Illahi Bakhsh Soomro. Risk factors and outcome in 114 young stroke patients. Med Channel Oct - Dec 2006;12(4):52-5.

Address for Correspondence:
Dr. Aamir Shahzad
136 Askari XI,
Street No.3, Cobbe lines